REMARKS

Claims

Claims 1–5 and 8–16 are currently under examination with claims 6–7 withdrawn from consideration due to restriction/election. Claims 17 and 18 are added by this paper.

Applicants acknowledge the allowability of claim 10.

Claim Amendments

The claims have been amended to use language in accordance with conventional US practice and do not raise new matter.

Rejection under 35 U.S.C. § 112, second paragraph

The rejection, not specifically discussed herein, is moot in view of the amendment. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-5 and 8, 9, and 11-6 stand rejected under 35 U.S.C. §112, first paragraph as allegedly being non-enabled. Applicants courteously traverse this rejection.

At page 3, the Office Action contends that since "the prior art has repeatedly taught that phosphoamidase, protein phosphoamidase, and protein histidine phosphoamidase, including PHP1 will only hydrolyze P-N bonds and is devoid of the activity of hydrolyzing P-O bonds," the unexpected hydrolysis of certain P-O bonds (as presented in page 11, lines 1–13 of the specification and the disclosure contained in Fig. 7 and Fig. 8) is non-enabled. See, last paragraph at page 4 of the Office Action. Applicants respectfully disagree with this contention.

At the outset, it is courteously submitted that insufficient evidence has been presented to support the generality of the aforementioned allegation that "histidine phosphoamidase, including PHP1, will only hydrolyze P-N bonds and is devoid of the activity of hydrolyzing P-O bonds." The Patent Office relies on Hiraishi et al. (1999) and Ek et al (2002) to support this contention. See, page 8, 2nd paragraph of the Office Action. However, both these publications do not recite the substrates employed herein. Hiraishi, as discussed previously, is drawn to glucose-6-phosphate and/or phosphotyrosine

substrates. Ek utilizes P-N and/or P-O linked amino acid substrates. Therefore, even if the PTO's reliance on the scientific disclosures of Hiraishi and Ek were correct, the Examiner's contentions on alleged lack of "true phosphoamidase" activity appear misplaced. The specific compounds of Hiraishi and/or Ek are not the subject matter of the instant invention, and more importantly, the cited references do nothing to demonstrate that the claimed assay would not work with the instantly claimed substrates. As the Examiner admits, "PHP1 did unexpectedly hydrolyze certain P-O bonded substrates [such as DiFMUP and FDP]." See, 1st paragraph at page 5 of the Office Action and the disclosure contained in Figs. 7 and 8 of the instant specification. This demonstrates that the prior art situation relied on by the Examiner is not true for the recited substrates and lends high credibility to the claimed process. There is no reason presented on which to doubt that the process will work in all five claimed substrates.

In order to support the claimed invention, Applicants' specification provides adequate written description of the term "protein histidine-phosphoamidase" and provides reference to candidate proteins which are commensurate with this description. For example, based on the instant specification, such proteins may constitute proteins that are capable of hydrolyzing phosphorylated basic amino acid residues such as histidine (P-His), lysine (P-Tyr) or arginine (P-Arg) within peptides or proteins. A representative example of the claimed "protein histidine-phosphoamidase" is PHP1, the structure/function of which is described in Applicants' own specification and the cited reference of WO 00/52175. See, page 4, lines 28-34.

It is therefore respectfully submitted that Applicants' specification, coupled with scientific references cited therein, provides adequate guidance on phosphoamidase enzymes and activity thereof. Applicants' specification provides adequate written description of the substrate molecules, regents, and assay conditions, which would allow a skilled artisan to both make and use the instant invention without undue experimentation. "To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation." Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)). For example, the instant specification provides numerous representative examples on methods for assaying for the activity of

such proteins using the claimed set of five substrates. See, *e.g.*, FIGS. 6–8 and the description of the figures provided at pages 7–8 of the specification. In short, the instant specification is fully commensurate with what is claimed by the Applicants' invention.

In view of the above remarks, it is respectfully submitted that Applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with an effort that is routine within the art. The statute requires nothing more. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejection under 35 U.S.C. §102(b)

The rejection of claims 1-3, 5, 8, 9, and 11-16 under 35 U.S.C. §102(b) as allegedly anticipated by Mountfort (1999) as evidenced by Kim is respectfully traversed.

In levying the anticipation rejection, the Office Action contends that "the assay method of the instant invention is not enabled for the detection of phosphoamidase" because the instant claims encompass protein histidine phosphatase and protein histidine phosphatase with phosphoamidase activity. It is further alleged that novelty is destroyed by Mountfort because Kim allegedly teaches that Mountfort's protein histidine phosphatase 2a has phosphoamidase activity. Applicants respectfully disagree with this contention.

The cited reference of Mountfort, Kim and Citation No. 2 (Molecular Probes) are drawn to the detection of hydrolysis of phosphate monoesters (P-O bonds) from various phosphor-ester metabolizing phosphatase enzymes. See, the first sentence of the 2nd paragraph in Section 10.3 of Citation 2 (Molecular Probes) and the disclosure contained in page 10, line 17 of the instant application. The cited reference of Kim provides a generic description of the phosphatase activity of PP1, PP2A and PP2C. Kim does not assay for the phosphoamidase activity nor employ any of the substrates claimed herein.

In summary, a skilled artisan would not have envisioned that a substrate with P-O bonds (phosphor-monoester) as claimed in Applicants' claim 1, would be suitable for the detection of enzyme activity of phosphor-amid metabolizing enzymes such as phosphoamidases. The skilled artisan would assume that a phosphoamidase enzyme would not be able to hydrolyze phosphopeptides with phospho-monoester (as disclosed in Figures 2 and 3 of the instant specification) and that this enzyme is not able to hydrolyze P-

O bonds in substrate like FDP, DDAO, DifMUP, ELF39, and ELF97.

It is therefore respectfully submitted that both Mountfort and Kim fail to teach or recite all the elements of Applicants' claims. Without such, there can be no anticipation. Furthermore, insofar as Mountfort and Kim are both silent as to the utilization of P-O bond hydrolysis as an assay for phosphoamidase activity, a combination of the cited references, even at their broadest interpretation, cannot render obvious the instantly claimed subject matter.

Withdrawal of the rejection is respectfully requested.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

No fees are believed to be due with this response; however, the Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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